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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/614,365
Filing Date: July 07, 2003
Appellant(s): MEADE ET AL.

John A. Sopp
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 23, 2007 appealing from the Office action mailed November 22, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6706726	Meissner et al.	03-2004
6060069	Hill et al.	05-2000

Knowles et al., PCT international Publication WO03/011274, filed 25 July 2002, published 13 February 2003, IPC classification A61K 31/192

(9) Grounds of Rejection

Applicant's terminal disclaimer, submitted March 22, 2007, disclaiming the terminal portion of any patent issuing from the instant application extending beyond the expiration date of any patent issuing from copending application 10/613783, filed with respect to the provisional rejection of instant claims 1, 2, 4, 5, 7, and 43 under the doctrine of obviousness-type double patenting as claiming the same invention as claims 1-13 of US application 10/613783 in view of claims 1-8, 11, and 21-23 of US patent 6706726, of record in the final rejection of November 22, 2006, has been fully considered and found to be persuasive to remove the rejection. Therefore the rejection is withdrawn.

The following ground of Rejection is applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 7-11, 13, 19-38, 43, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knowles et al. (PCT international publication WO03/011274, of record in previous action) in view of Meissner et al. (US patent 6706726, of record in previous action) further in view of Hill et al. (US patent 6060069, of record in previous action) Note that The Meissner et al. patent is an English equivalent of foreign patent DE 10050994, published 18 April, 2002. This rejection is set forth in the prior office action of November 22, 2006, reiterated in full below.

Knowles et al. discloses combinations of an anticholinergic and a PDE-4 inhibitor and methods for their use in preventing or reducing the symptoms of pulmonary disease. (p. 1, lines 1-7) Theophylline is mentioned as an example of a PDE-4 inhibitor, although any PDE-4 inhibitor may be included within the scope of the invention. (p. 3, lines 25-26) An example is provided of a pharmaceutical dose formulation which comprises a 1:1 ratio of cliomilast and tiotropium bromide, an anticholinergic, in 18 µg each in a metered dose inhaler with 1,1,1,2-tetrafluoroethane, also known as TG134a, (p. 10, table 1, lines 4-9) falling within the limitations of instant claims 8-13 and 19-22 for use in an inhaler according to instant claim 40. Another embodiment is a powder formulation for a dry powder inhaler comprising cliomilast and tiotropium bromide mixed

with lactose as an excipient, (p. 10, lines 10-19) in the limitations of instant claims 11-14, enclosed in a hard gelatin capsule and enclosed in an inhaler according to instant clams 14, 17 and 40. The formulation for nasal administration described on p. 10, lines 20-29 contains hydrochloric acid, a pharmaceutically acceptable inorganic acid according to instant claim 44. Knowles et al. does not disclose a pharmaceutical combination comprising **1** and a PDE-4 inhibitor. Knowles et al. also does not disclose an inhalable powder having a particle size of up to 250μm or between 10 and 150μm, as described in instant claims 15-16 or an inhalable powder comprising only **1** and **2** as described in instant claim 18, or a propellant containing inhalable aerosol containing additional ingredients according to instant claim 23, or a propellant-free inhalable solution according to instant claims 25-38.

Meissner et al. discloses anticholinergic compounds of a general formula which includes **1** as an embodiment. (Example 1, column 10, lines 10-29) These agents are expected to be useful in the treatment of chronic obstructive pulmonary disease and asthma. (column 19, lines 63-65) Meissner et al. specifically discloses that these compounds may be administered by inhalation. (column 22, lines 26-29) Specific formulations described by Meissner et al. include an aerosol spray for use in an inhaler, (column 24, lines 40-55) an inhalable solution according to instant claims 25-29, 32, 33, 36, and 39 for use in an inhaler according to instant claim 42, (column 24, lines 58-67) and a powder comprising the active substance and lactose monohydrate. (column 25, lines 15-20)

Hill et al. discloses a method of treating pulmonary disease by administering a drug as an inhalable powder using lactose as an excipient, in which the lactose particles are in the size range of between 20 and 100 microns. (column 3, lines 38-46)

It would have been obvious to one of ordinary skill in the art at the time of the invention to produce a composition similar to those disclosed by Knowles et al. comprising the anticholinergic drug of Meissner et al. in place of the anticholinergics disclosed by Knowles et al and to use this combination in the therapeutic method of claim 43. It would also have been obvious to one of ordinary skill in the art to prepare this composition as an inhalable powder comprising the active ingredients and lactose with a particle size of between 20 and 100 microns as described by Hill et al, or an inhalable powder comprising only **1** and **2**. It would furthermore have also been obvious to prepare the pharmaceutical composition as a propellant-containing aerosol containing additional ingredients as described in claim 23, or as a solvent-free inhalable aerosol as described in claims 25-39.

One of ordinary skill in the art would have been motivated to prepare the composition using the anticholinergic compound **1** of Meissner et al. in place of the anticholinergics of Knowles et al. because this compound is also an anticholinergic, is structurally similar to the compounds of Knowles et al., and is useful for treating the same condition. (i.e. obstructive pulmonary disease) One of ordinary skill in the art would have been motivated to prepare the composition as an inhalable powder additionally comprising lactose with a particle size of between 20 and 100 microns because a similar composition is disclosed by Hill et al. for the pulmonary delivery of a

different drug. One of ordinary skill in the art would have been motivated to prepare an inhalable powder containing only **1** and **2**. because the lactose excipient is an inert carrier which is not essential to the biological function of the active ingredient. One of ordinary skill in the art would have been motivated to prepare a propellant-containing aerosol containing additional ingredients as described by claim 23 because adding standard ingredients such as preservatives, stabilizers, and surfractants is standard practice in the art. One of ordinary skill in the art would have been motivated to prepare the composition as a propellant-free aerosol according to claims 25-29, 32, 33, and 36 because Meissner et al. discloses such a solution as a means for pulmonary delivery of the anticholinergic. One of ordinary skill in the art would have been motivated to add to this solution a co-solvent according to claims 30-31 and to add an antioxidant because determining the exact solvent composition and excipients of a pharmaceutical composition is a routine procedure in the art. One of ordinary skill in the art would have been motivated to use sodium EDTA in this solution because Meissner et al. discloses a solution comprising EDTA and sodium EDTA is a common form of EDTA. One of ordinary skill in the art would have been motivated to prepare the solution with only benzalkonium chloride or benzalkonium chloride and sodium EDTA because these solutions consist essentially of the same ingredients as the propellant-free solution disclosed by Meissner et al. and differ only in the absence of HCl, which is not essential to the biological function of the active ingredient.

One of ordinary skill in the art would have reasonably expected success in preparing the pharmaceutical composition with the compound of Meissner et al.

because of the similarities between this compound and those already known to be useful in this invention. One of ordinary skill in the art would reasonably have expected success in preparing an inhalable powder with a particle diameter between 20 and 100 microns and an inhalable solution according to claims 25-29, 32, 33, and 36 because these formulations are taught in Meissner et al. and Hill et al. to be useful for pulmonary delivery of drugs. One of ordinary skill in the art would have been motivated to make various minor modifications such as adding ingredients as described by claims 23, 30, 31, 34, and 35 or subtracting them as described in instant claims 18, 36, and 37 because these modifications are minor modifications which are well within the routine skill of one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

(10) Response to Argument

Claim Rejections - 35 USC § 103 Maintained

The only limitation addressed by Appellant is the motivation and expectation of success in combining the two claimed active agents, namely an anticholinergic and a PDE-IV inhibitor.

Appellant argues that one of ordinary skill in the art would have no motivation to use the compounds of Meissner in combination with a PDE-IV inhibitor as discussed by Knowles. In particular, it is asserted that Knowles teaches no anticholinergic compounds that fall within the limitations of the instant claims, and that the compounds disclosed by Meissner are sufficiently different from those of Knowles that one of

ordinary skill in the art would not expect them to be useful in combination with the PDE-IV inhibitors revealed by Knowles. Appellant details several structural differences between the claimed compounds and those of Meissner, as well as alleged differences in the structural selectivity of the different compounds.

First, it is noted that both references describe the disclosed compounds and compositions as being useful for treating the same disorders, notably asthma and chronic obstructive pulmonary disease. The mere fact that two compositions are useful for the same purpose is sufficient to provide a *prima facie* case for the obviousness of the combination.

Secondly, both the compounds described in Knowles and those described by Meissner are disclosed as anticholinergic agents. Because of this shared activity, there is a *prima facie* case of obviousness for the substitution of one compound for another. The structural similarity between the two compounds merely serves to provide additional evidence that they are expected to be interchangeable and is not seen to be essential for a finding of obviousness.

As regards the specificity of the anticholinergic compounds for the M1, M2, or M1/M2 receptors, as revealed on p. 2, lines 32-36 of Knowles et al., the fact that both classes of compounds produce the disclosed anticholinergic effects and therapeutic utility is seen to be sufficient to provide a rationale for combining them, regardless of whether Meissner specifically discloses that the compounds have the same receptor specificity. It is clear from the section Summary of the Invention on p. 2, lines 13-31 of Knowles et al. that Knowles, in its broadest embodiment, covers combinations of a

PDE-IV inhibitor with an anticholinergic agent generically. The "fifth aspect" disclosed in lines 32-36 is a preferred embodiment that is not absolutely required for the invention of Knowles et al. According to MPEP 2123, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." See In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) 27 F.3d at 554, 31 USPQ2d at 1132.). 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Finally, Applicant argues that Meissner directs one of ordinary skill in the art away from interchanging the two compounds by stating that the benzylic acid esters described by Knowles et al. are inferior and deficient in meeting the requirements of the invention. However, this information actually supports the substitution of the superior compounds of Meissner for the inferior compounds of Knowles. When one compound is shown to be superior for a particular purpose to a prior art compound, this information provides a clear motivation for substituting the superior compound for the inferior compound.

The record contains no clear and convincing factual evidence of nonobviousness or unexpected results, i.e., testing data for the combination method herein over the prior art. In this regard, it is noted that the specification provides no side-by-side comparison

with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art.

(11) Related Proceedings Appendix

No decision rendered by a court or the board is identified by the examiner in the Related Appeals and Interferences sections of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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10/23/07

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